

Discontinuation of antiviral drugs may be the reason for recovered COVID-19 patients testing positive again

Introduction

Currently, some patients in China who have been treated for COVID-19 and discharged from hospital have tested positive again in subsequent nucleic acid tests. The authors believe that discontinuation of antiviral drugs may be one of the reasons for recovered patients with COVID-19 testing positive again.

Case report

A 46-year-old woman, who had come into close contact with a patient who had COVID-19 10 days earlier, developed a dry cough, throat discomfort and fatigue 5 days before admission. The patient had a history of good physical health with no underlying disease. The patient's temperature and physical examination were normal. Laboratory analysis results showed reduced white blood cell count ($2.9 \times 10^9/\text{litre}$), neutrophil count ($1.8 \times 10^9/\text{litre}$) and platelet count ($56 \times 10^9/\text{litre}$), but lymphocyte count, C-reactive protein levels and biochemical indices were within normal ranges. Her throat swab nucleic acid was positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by real-time reverse transcriptase polymerase chain reaction assay. On 9 February 2020, she was diagnosed with mild COVID-19.

On 10 February, 1 day after admission, computed tomography showed multiple patches and increased flocculent density in the lower lobe of both lungs, mainly distributed under the pleura, with blurred borders. She was given oxygen inhalation, antiviral therapy (lopinavir/ritonavir 400 mg twice daily by mouth, recombinant human interferon $\alpha 1b$ 50 μg twice daily inhaled, ribavirin 0.5 g twice daily intravenously). On 17 February, computed tomography showed that the range and density of lesions had increased in the left lower lobe. On 20 February, a chest computed tomography scan revealed ground glass opacities had been clearly absorbed in both lungs. At the same time, her nucleic acid test from her throat swab was negative on 19 and 20 February, and her clinical symptoms improved significantly. The discharge criteria of the 'Guidelines of COVID-19 (trial version 6)' (National Health Commission of the People's Republic of China, 2020a) are as follows:

1. Body temperature returned to normal for more than 3 days
2. Respiratory symptoms improved significantly
3. Inflammation of the lungs showed obvious signs of absorption
4. Respiratory nucleic acid was negative on two consecutive times (with samples taken at least 1 day apart).

The patient met the discharge criteria, and lopinavir/ritonavir and ribavirin were discontinued. On 23 February, her nucleic acid test from her throat swab was still negative, but 3 days later, her nucleic acid test reversed to positive, and chest computed tomography revealed that the lesion in the right lower lobe was almost completely absorbed, but the range and density of lesions in the left lower lobe had increased compared with those seen 6 days earlier (26 February). Since her symptoms were only a slight dry cough, she continued aerosol inhalation of recombinant human interferon $\alpha 1b$. On 29 February and 1 March, nucleic acid tests from her throat swab were both negative. On 2 March, chest computed tomography showed absorption and dissipation of bilateral lung lesions, and she was discharged from hospital.

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Learning points

- After discontinuation of antiviral drugs, some patients whose lung lesions have not been completely absorbed may test positive for COVID-19 again.
- When considering discontinuing antiviral drugs for COVID-19 patients, particularly those who have no obvious clinical symptoms, it is important to not only consider the patient's viral nucleic acid test results, but also the manifestations on chest computed tomography.

Discussion

In China, some patients who have had COVID-19 but been discharged have tested positive again in later nucleic acid tests (Foreign Affairs Office of Tianjin Municipal People's Government, 2020). Six days after this patient reached the discharge standard, her nucleic acid test showed up as positive. Xie et al (2020) mentioned that reasons for false negative real-time reverse transcriptase polymerase chain reaction results may include insufficient cellular material for detection and improper extraction of nucleic acid. However, the authors strictly adhered to the guideline of viral nucleic acid testing (Version 2) (National Health Commission of the People's Republic of China, 2020b) and collected two throat swabs at a time to ensure that sufficient cellular material was obtained. The patient had negative results on 19, 20 and 23 February. The patient's nucleic acid test results were consistent with imaging changes. After lopinavir/ritonavir and ribavirin were discontinued, the exudation in the left lower lobe increased slightly on computed tomography and the nucleic acid test result returned to positive. Hence the authors concluded that the possibility of a false negative real-time reverse transcriptase polymerase chain reaction result was small. Quarantined in an isolation room, the patient was protected from subsequent exposure, so the authors believe that this excludes the possibility of a second infection. Unfortunately, there are no genotype data to show whether or not the isolated virus on the second occasion was indistinguishable from that on the first.

The authors concluded that after antiviral drugs have been discontinued in some patients, the residual virus causes the pulmonary lesions to re-aggravate, resulting in subsequent positive viral nucleic acid test results.

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